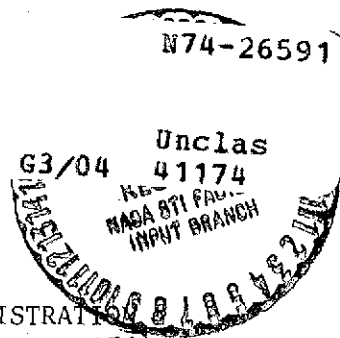


CARDIAC OUTPUT AND OXYGEN INTAKE AT REST AND DURING
SUBMAXIMAL LOADS ON 8-14 YEAR OLD BOYS.

R. Mocellin, W. Sebening and K. Bühlmeier

Translation of: "Herzminutenvolumen und Sauerstoffaufnahme
in Ruhe und während submaximaler Belastungen
bei 8--14jährigen Jungen,"
Z. Kinderheilk., 114, 1973, pp. 323-339.]

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16. Abstract Cardiac output, oxygen intake, and heart rate were measured in 22 boys of ages 8 to 14 at rest and under application of two submaximal loads on the bicycle ergometer. The arteriovenous oxygen difference, stroke volume, and oxygen intake per kilogram of body weight were calculated from the measured values. The measured values were compared with values recorded in other studies with adults and older children and with the values expected on the basis of theory.			
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CARDIAC OUTPUT AND OXYGEN INTAKE AT REST AND DURING
SUBMAXIMAL LOADS ON 8-14 YEAR OLD BOYSR. Mocellin, W. Sebening and K. Bühlmeier¹

Experiments on the reaction of the cardiovascular system to physical stress have been conducted among adults for about 15 years. Consequently, the problem of pulmonary hypertension with vitium cordis in the left-right shunt (admixture of arterial and venous blood) was emphasized at the outset. So Swan et al., discovered a decline of shunt capacity while under stress among those patients in whom pulmonary hypertension had previously continued at rest, with only a slight rise in pulmonary blood flow. The conclusions of Bruce and John, however, as well as Davies and Gazetopoulos, have shown that among such patients there is a relatively stronger increase of pulmonary circulation output with progressive stress owing to the rise in shunt output, while cardiac output remained relatively low in systemic circulation with rising pressure.

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Petersson was the first to conduct hemodynamic experiments on stress among children suffering from heart disease. Subsequently, the problem arose of there not being sufficient research on the reaction of cardiac output among healthy children under stress, so that Petersson drew into his comparison values from healthy adults. Until 1969, only 2 experiments on altogether 5 children on hemodynamic variations during physical stress among healthy children and adolescents had been conducted, as far as we know; among them various foreign gas methods had been employed for determining cardiac output.

In 1929, Galle discovered extraordinarily low values of cardiac output, compared with the values of adults, among 2 twelve year old boys by means of the Krogh and Lindhard nitrous oxide method, at rest as well as in a relatively low-stress situation (Figure 1). In contrast, in 1936 Schneider and Crampton

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*Numbers in the margin indicate pagination in the foreign text.

found no irregular reaction in cardiac output at rest and in rising values of oxygen intake among 3 boys in puberty with the assistance of the Grollman acetylene method when one compares the conclusions with those obtained from young adults (Figure 1).

The dearth of research on the circulatory behavior of children under stress which existed until quite recently may essentially be explained by the fact that we have only reluctantly decided on using sanguineous methods, which at present assist in the determination of cardiac output, on children.

New possibilities resulted from the application of the indirect Fick Method, inaugurated by Douglas and Haldane, and the CO_2 rebreathing method, which meanwhile could be perfected through technical developments. By means of this method, Godfrey and others ascertained the cardiac output among 6-15 year old boys and girls during submaximal and maximal stress on the bicycle ergometer, and found in general that somewhat lower values than those of the young adults tested by Ekblom et al., as well as Bevegård et al., (1960), were indicated in relation to O_2 intake. It followed from their research that among the test group smaller children with the same O_2 intake exhibited somewhat lower values in cardiac output than larger children. /326

Also, with the aid of the CO_2 rebreathing method, Bar-Or et al., discovered extraordinarily low stress values in cardiac output among 10-13 year old boys (Figure 1) and girls, whereby in contrast to the conclusions of Godfrey et al., a sex-related differential occurred in such a way that on the average the values for boys fell below those for girls.

By reason of contradictory conclusions, it became obvious that controlled experiments ought to be conducted using the Pigmentary Rarefaction Method. Eriksson and others discovered cardiac output values among 13-14 year old boys which were in the lower normative range of the stated connection between oxygen intake and cardiac output for adults. Eriksson and Koch succeeded in coming to similar conclusions with tests on 11-13 year old boys. We considered it expedient to conduct further experiments, including younger children, in order to clarify these correlations, which are of particular clinical interest.

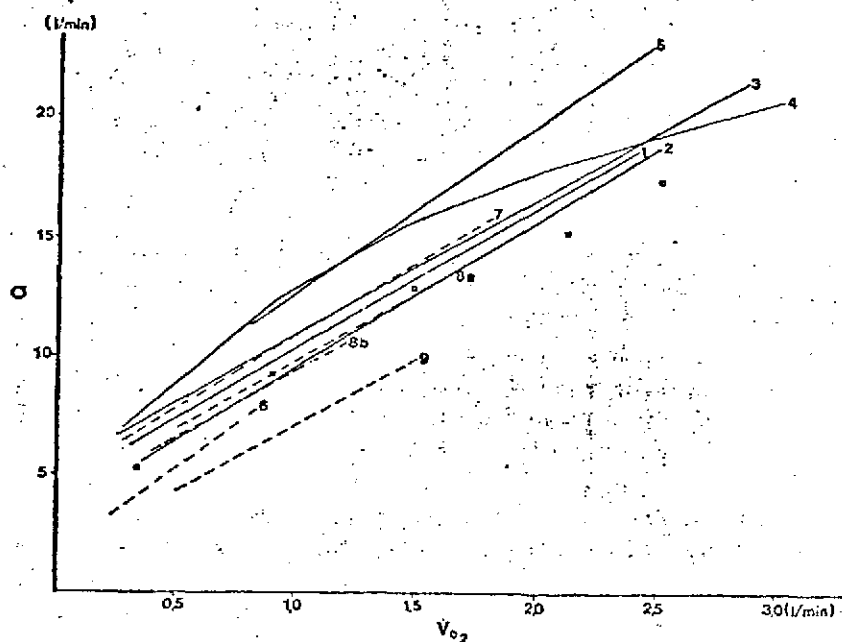


Figure 1. The Dependence of Cardiac Output (Q) on Oxygen Intake (V_{O_2}) in Young Male Adults (Solid Lines) as Well as Children and Adolescents (Dotted Lines) In Upright Position. [1]-Bevegård et al., (1960). [2]-Reeves et al. [3]-Ekblom et al. [4]-Asmussen and Nielsen. [5]-Dill et al., as well as Bock et al., cited by Becklake et al., [6]-Galle. [7]-Schneider and Crampton. [8] (a), (b)-Godfrøy et al., (both curves were calculated according to the average body lengths of our test subjects in both age groups from the formulas specified for boys by the authors (a)--according to a body length of 154.2 cmn, (b)--according to a body length of 137.7 cm). [9]-Bar-Or et al. Average values of Eriksson et al., (13-14 year old boys).

I. Methodology

1. Research Data

Boys in the 8-14 age range took part in our experiments, and they came into our cardiology outpatient clinic on a regular basis for the controlled experiments. All the children had suffered the symptoms of a heart murmur for years, thus making it impossible to make any firm determination on the basis

of clinical research as well as with the roentgenogram whether it was a question of an accidental murmur or a small defect in the septum of the auricle. For final clarification, dextral-cardiac catheter research was undertaken. In subsequent research only those children, 22 in all, in whom a cardiac defect could be excluded were taken. The parents and the children were informed prior to the course of the research and had given their permission. No premedication was administered.

Upon the termination of the experiments, the boys were subdivided into two age groups of 8-11.5 and 11.5-14, respectively. Table 1 gives the standard value and standard deviations for age, body length, and body weight in these two age groups. From a comparison with the normative values of Meredith, it follows that the children we tested exhibit average length and body development. The vast majority of the children participated in school sports, and a few pursued team sports.

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Table 1.

	The younger group, 8-11.5 years old.	The older group, 11.5-14 years old.
Age in years	9.4 \pm 1.2	12.8 \pm 1.0
Body length (cm)	137.7 \pm 5.7	154.2 \pm 12.3
% ASL	100.5 \pm 3.4	100.6 \pm 4.4
Body weight (kg)	30.2 \pm 5.2	43.3 \pm 10.1
% ASG	98.6 \pm 14.7	100.7 \pm 14.6

Table 1. Average Values and Standard Deviations in Age, Body Length, and Body Weight of the Test Subjects. The data on body measurement were compared with the norm values of Meredith (% ASL equals the percentage of theoretical length for that age, % ASG equals the percentage of theoretical weight for that age).

2. Experimental Setup

The research was undertaken on an outpatient basis. The children were brought to the clinic in the morning, after breakfast. There, as an orientation

experiment, the determination of the W_{170} , or the output with a pulse frequency 170 min^{-1} , and also with a gradually rising output according to Bengtsson's Proposition, was completed. Next, the children were familiarized with the spirometric experiment. After a short rest period, following a local anesthetic to the vena cubitalis of the left arm, the catheter experiment on the right side of the heart with concomitant measuring of pressure and oxygen saturation in various heart and blood vessel segments was conducted, and any active failure of the shunt in the test subjects was suspended. After shutting off the heart catheter, a Ch. 6 or 7 Cournand-catheter was inserted into the superior vena cava and fastened. Moreover, the arteria brachialis of the left arm was exposed and punctured under a local anesthetic. Thereupon followed a rest period of about 45 minutes in a reclining position, at the beginning of which the children could, if they wished, eat and drink a little.

Next, measurements of oxygen expenditure and cardiac output, as well as heart rate, were taken on the bicycle ergometer, first at rest and then at any given time in two 6-minute uninterrupted load application stages. The stresses were measured in such a way that a heart rate of 170 min^{-1} was reached approximately on the second stage. The measurements during the stresses were taken between the 5th and 6th minutes, i.e., after the achievement of a relatively steady state, specifically the measurement of oxygen expenditure over 2 minutes and the measurement of cardiac output in repeat determinations were taken. The cardiac output was telemetrically transmitted and continuously registered during the entire experiment.

Upon completion of the experiment the venous catheter as well as the arterial puncture tube were removed and both blood vessels were closed with sutures. After another 2-hour rest period the children were sent home.

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3. Measuring Equipment

To measure output we employed a bicycle ergometer which was independent of rotational speed (manufactured by the Elema Firm), with a tread velocity of about 60 pedal revolutions per minute held constant. The telemetric transmission of EKGs was accomplished with the help of a system manufactured by Hellige. A printing device was kept above the right flip of the EKG, and it automatically printed in full the total pulse after a 1-minute lapse.

The exhaled air was collected in a Douglas Sack during the 4-6 minute rest periods, and for every output stage during the last two minutes. The volume of the exhaled air was determined with a dry gas meter, and the analysis of the respiratory air ensued with the use of the infrared absorption principle for CO₂ and the paramagnetic one for O₂. We used cardiogreen as the indicator material for determining cardiac output. The measurement itself was conducted with a cardiodiagnostic densitometer, which was calibrated at the conclusion of a complete experiment. Altogether, perhaps 20-30 ml of blood were drawn and, for the purpose of calibration, around 20 ml were drawn at the conclusion of the experiments in order to determine the oxygen saturation values during the heart catheter test.

4. Applied Statistical Methods

Arithmetic averages, distribution, factors for rate correlation, and regressions of the first type were determined, with only a few accidental variations, according to well-known statistical procedures. The computations of the standard error of regressions follows the formula:

$$s_{y \cdot x} = \sqrt{\frac{\sum (y - \bar{y})^2 - \sum (x - \bar{x})^2 \cdot b^2}{n - 2}}$$

We completed the test of two even numbers on identity with the aid of the "t"-test, according to formula No. 685 in the chapter on statistics of "Documenta Geigy -- Wissenschaftliche Tabellen", (The Scientific Tables) (Sixth ed., 1962).

II. Findings

In Table 2, for both of the tested age groups, we have separated the mean values and standard variations of the calculated parameters we measured respectively from the values measured during seated rest, and we have reproduced them on 2 submaximal output stages (specific values from Sebening). The stresses were chosen in accordance with the results from the prior determination of the W₁₇₀ in such a way that a heart rate of 170 min⁻¹ would be attained.

It is noteworthy here that the relative weight-related values for oxygen intake (V_{O_2}/KG) differed on the average only insignificantly in both age groups during rest and in both stages of stress. A corresponding reaction also showed the mean values of arteriovenous oxygen difference and cardiac rate in both age groups. In contrast, the variations in volumes of cardiac output, which were small only at rest, and those in the absolute values of oxygen intake between younger and older children, increased with the relative stress.

The average output differed widely between the two age groups at rest. This difference still increased with stress. Here both groups reacted somewhat differently insofar as the volume of output was practically identical for both stages of stress, i.e., with younger children, while with older children a small rise in output volume still ensued from the 1st to the 2nd stage of stress.

The behavior of individual parameters is made clear in Figure 2, in which volumes of cardiac output (Q), cardiac rate (HF), the arteriovenous oxygen differential ($A-V_{O_2}$ diff.), and also output volumes of both age groups were all fixed with respect to relative oxygen intake (V_{O_2}/KG). This indicates that in both age groups there is a linear connection between oxygen intake per kilogram of body weight on the one hand and volumes of cardiac output as well as cardiac rate on the other, while the connection between relative oxygen intake and the arteriovenous differential describes an approximately hyperbolic curve.

Accordingly, there is no linear correlation between cardiac rate and arteriovenous oxygen differential, as follows from Figure 3. In both age groups, the curve has a much greater similarity with the same one between relative O_2 intake and arteriovenous differential.

In Figure 4, the regressions between oxygen intake and volumes of cardiac output for both age groups, which have been calculated from the values specified by Ekblom et al., for young adults, has been rendered in the form of a dotted line. For a better understanding of the relationships, several lines of identical arteriovenous O_2 difference have been drawn in as well.

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		The younger group, 8-11.5 years old	The older group, 11.5-14 years old
\dot{V}_{O_2} [l/min]	R	0,22 \pm 0,03	0,27 \pm 0,07
	I	0,61 \pm 0,10	0,87 \pm 0,23
	II	0,97 \pm 0,16	1,33 \pm 0,34
Q [l/min]	R	4,5 \pm 0,6	5,8 \pm 1,5
	I	7,3 \pm 0,7	10,0 \pm 2,0
	II	9,6 \pm 1,0	13,2 \pm 3,0
HF [min ⁻¹]	R	93 \pm 16	91 \pm 11
	I	130 \pm 11	135 \pm 16
	II	169 \pm 7	167 \pm 11
SV [ml]	R	50 \pm 9	64 \pm 16
	I	56 \pm 9	76 \pm 15
	II	57 \pm 5	81 \pm 17
$A-V_{O_2}$ -Diff. [ml/100 ml]	R	5,0 \pm 0,9	4,8 \pm 1,5
	I	8,4 \pm 1,4	8,7 \pm 1,8
	II	10,1 \pm 1,4	10,3 \pm 2,5
\dot{V}_{O_2}/KG [ml/min/kg]	R	7,2 \pm 0,7	6,2 \pm 0,8
	I	20,3 \pm 3,7	20,2 \pm 4,1
	II	32,5 \pm 5,9	30,8 \pm 4,9

*Note: Commas denote decimal points.

Table 2. Standard Values and Standard Deviations for Oxygen Intake (\dot{V}_{O_2}), Cardiac Output (Q), Heart Rate (HF),

Output (SV), Arteriovenous Oxygen Differential ($A-V_{O_2}$ -diff.), and the Oxygen Intake Per Kilogram of Body Weight (\dot{V}_{O_2}/KG) at Rest (R), as Well as During Two Stages of Stress (I, II²) in Both Age Groups.

It follows that the values for cardiac output volumes with varying values of oxygen intake in the group of older children are in essence only slightly below those of young adults, and they even attain them with higher values of O_2 intake. On the other hand, the volumes of cardiac output for younger children in the whole range of the reproduced correlation clearly lie below the values of adults, as also below those for older children. The curve of the relationships in both age groups is somewhat more steep than with adults, although together the curves of the younger children and the older ones we tested run nearly completely parallel, whereby the difference in cardiac output volumes

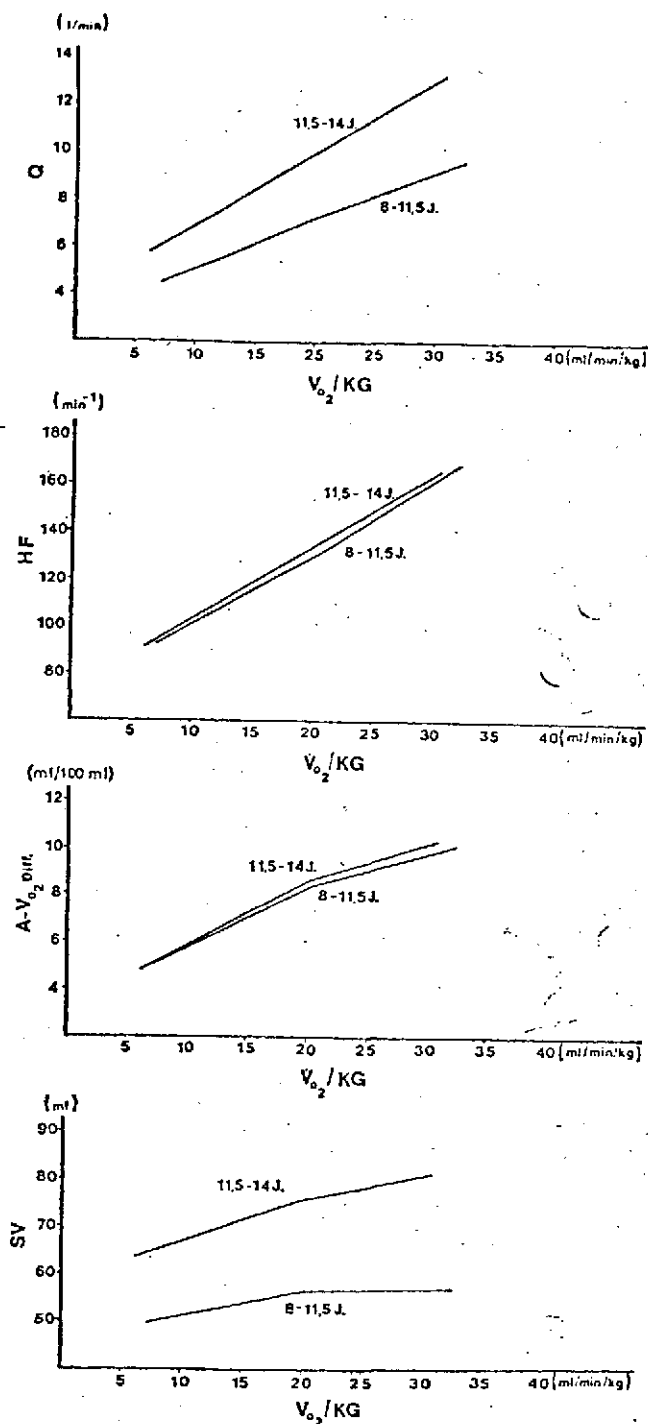


Figure 2. The Relationships Between Cardiac Output (Q), Heart Rate (HF), the Arteriovenous O_2 Differential ($A-V_{O_2}^{diff.}$), as Well as Output (SV) on the One Hand and the Oxygen Intake per Kilogram of Body Weight (V_{O_2}/KG) on the Other Hand With Boys of the Two Age Groups.

with identical values for O_2 intake amount to something more than 1 l/min on the average.

In Table 3, the regression equations of both groups for the relationships between O_2 intake and volumes of cardiac output are reproduced. Moreover, the standard error of regressions and the correlation factor have been computed. By means of the "t"-test it was found during the investigation that both lines differ significantly on the $p < 1\%$ level, and consequently are not statistically identical. The relatively high standard error of regressions among older children is noteworthy. This error is explained chiefly by the extremely variable condition of body development in this group as compared with younger children (Table 1).

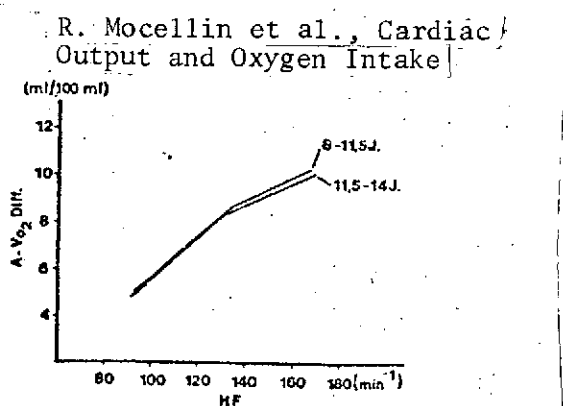


Figure 3. The Relationships Between Arteriovenous O_2 Differential (A-V O_2 -diff.) and Heart Rate (HF) With Boys of the Two Age Groups.

Table 4 includes the mean values of W_{170} determinations in both age groups, i.e., from the experiments both before and during the simultaneous determination of cardiac output volumes and oxygen intake. One should recognize that the W_{170} values during the experiments with sanguineous measurements are on the average about 10% lower than those in the preliminary investigations.

III. Discussion

If One wishes to compare the results we found with the obvious ones from the literature, it would seem appropriate to advance some theoretical considerations. We might proceed from such research, in which stresses as well as submaximal ones were pursued.

Judging by the nearly unanimous statements, with a determination of maximal O_2 intake male adults achieve an arteriovenous O_2 difference of 13.5-14.5 ml/100ml (Saltin et al.; Ekblom et al.; Rowell; Hartley et al.).

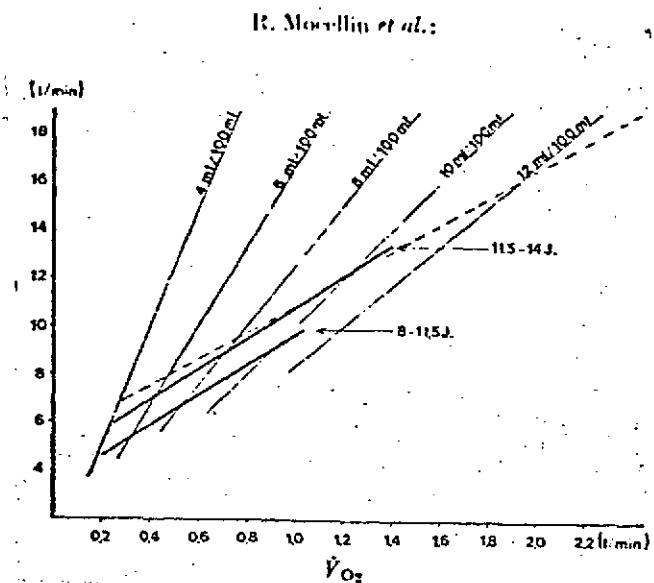


Figure 4. Dependence of Cardiac Output (Q) on Oxygen Intake (V_{O_2})

With Boys from Both Age Groups. The relationship calculated for young adults using the values of Ekblom et al., is drawn in as a dotted line. The set of graphs converging on zero includes lines of the same arteriovenous O_2 differential.

hand, it is almost universally known that, from the great number of experiments, the maximum O_2 intake per kilogram of body weight among male children and adolescents independent of age is about 45-50 ml/min/kg (Robinson; Bink and Wafelbakker; Lange-Andersen et al.; Mocellin and Wasmund; Eriksson -- there is also a comprehensive description of the literature values). Equal values of maximum O_2 intake per kilogram of body weight conform to equal values of maximum arteriovenous O_2 differential among male children and adults.

Table 3.

	The younger group, 8-11.5 years old	The older group, 11.5-14 years old
Regression equation	$Q = 3.3 + 6.4 V_{O_2}$	$Q = 4.3 + 6.5 V_{O_2}$
Standard error of regression	$s_{y \cdot x} = 0.77$	$s_{y \cdot x} = 1.93$
Correlation factor	$r = 0.941$	$r = 0.863$

For a long while, whether children could attain it relative to the high value of the arteriovenous oxygen differential with maximum stress was a topic for discussion. In 1952, through measurements of the oxygen pulse among children and adolescents, Astrand concluded that the arteriovenous O_2 differential could rise to 14.5 ml/100 ml, assuming a constant output during mean or maximal values for O_2 intake. The proportion of hemoglobin in the blood and the fact that the O_2 capacity among children is lower than among male adults seem to argue against this.

Through the work of Eriksson, Eriksson et al., as well as Eriksson and Koch, it has now been proven that boys of the 11-14 age group can attain the same maximum values in arteriovenous difference as can adults. On the other

Table 3. Regression Equations, Standard Regression Errors, and Correlation Factors for the Relationships Between Oxygen Intake (V_{O_2} [l/min]) and Cardiac Output (Q[l/min]) in Both Age Groups.

Both regressions differ significantly with a statistical error probability of $p < 1\%$.

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Table 4.

	The younger group, 8-11.5 years old $n = 10$	The older group, 11.5-14 years old $n = 12$
$W_{170} \text{ I [Watt]}$	$71,8 \pm 10,8$	$105,8 \pm 30,0$
$W_{170} \text{ II [Watt]}$	$65,3 \pm 12,3$	$96,2 \pm 24,4$

Table 4.. Average Values and Standard Deviations of the W_{170} Determinations Before ($W_{170} \text{ I}$) and During ($W_{170} \text{ II}$) the Experiments With Simultaneous Determination of Cardiac Output.

By reason of theoretical considerations, it may be anticipated that universal values of arteriovenous O_2 differential are reached with the same percentage values of maximum O_2 intake by children and adults. According to Fick's Principle, this means that children exhibit smaller volumes of output with the same absolute values of O_2 intake than do adults, and, indeed, it always becomes greater as the children become younger.

In order that we may be more accurately informed of these expected orders of magnitude of the differences by reason of this hypothesis, we have calculated the maximum O_2 intake (l/min) in various age groups, proceeding from the average values of body weight (Meredith), whereby we took a value of 45 ml O_2 /kg body weight as a basis. Proceeding from these values, we have introduced the actual point of intersection with a line, in relation between O_2 intake and cardiac output (Figure 5), perpendicular to the abscissa, upon which all points with an arteriovenous differential of 13.5 ml/100 l lie.

We made special use of this value as the maximal arteriovenous difference because the group of young adults tested by Ekblom et al., whose regression in Figure 5 is once again noted for comparison, achieved a maximal O_2 difference of

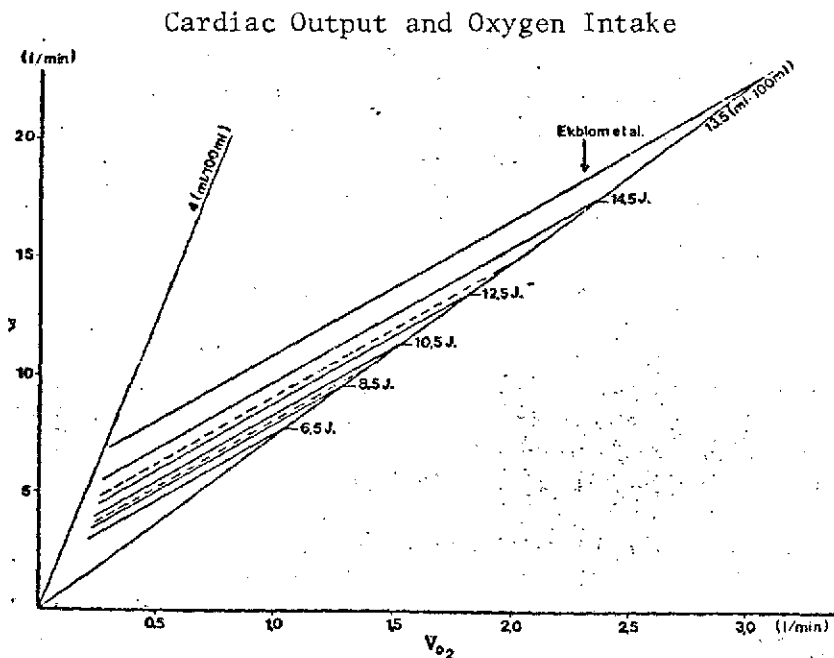


Figure 5. Hypothetical Curves of the Relationships Between Cardiac Output (Q) and Oxygen Intake (V_{O_2}) in Various Age

Groups of Boys. The maximal values were calculated according to a maximal O_2 intake of 13.5 ml/100 ml. Proceeding from the calculated values, the curves were plotted parallel to the correlation calculated with the values of Ekblom et al. In the same way, the straight dotted lines are determined for both of the groups of boys we tested with respect to body weight.

13.5 ml/100 ml. Proceeding from these named points of intersection with this line of identical arteriovenous O_2 difference, it became possible to introduce the hypothetical relationships between O_2 intake and cardiac output in the various age groups parallel to the regression which was calculated from the values of Ekblom et al. In the same way, the maximal O_2 intake was also calculated for both of the groups tested by us according to average body weight, and the temporary hypothetical regression between O_2 intake and cardiac output was introduced as a straight dotted line in the figure.

Figure 5 may be viewed as a good orientation aid for evaluating the conclusions of different research and also our own methods, if the assumption is valid that the relationships between O_2 intake and cardiac output are distinct

age groups run on a somewhat parallel course. The more recent results of Eriksson et al., as well as Eriksson and Koch, speak for this hypothesis.

In general, there exists a sound agreement between the values of Eriksson et al., for 13-14 year old boys and the hypothetical progress of the connection of 14 year old boys (Figures 1 and 5). So the relationship for the older age group of our boys, as it follows from the formula specified by Godfrey et al., was only displaced a little over the anticipated curve (Figures 1 and 5), while for the younger groups the relationship calculated by Godfrey et al., has shifted clearly in the direction of a greater volume of cardiac output in opposition to the straight reference line. This bespeaks the fact that the inclusion of body development in the formula mentioned by Godfrey et al., is not sufficiently taken into account. The volumes of cardiac output mentioned by Bar-Or et al., likewise determined with the help of the CO₂ rebreathing method, lie far below the values expected for 6 year old boys, so that a methodological error cannot be excluded (Figure 1 and 5).]

The relationships we ascertained in both groups between O₂ intake and volumes of cardiac output are shifted in the direction of lower volumes of cardiac output are shifted in the opposition to the values of Ekblom et al., but the values for volumes of cardiac output in both groups are, on the average, perhaps 1.5 l/min over the theoretically expected values (Figures 4 and 5). Against this a difference in the volume of cardiac output between both groups of perhaps 1 l/min in all stages of O₂ intake corresponds to the theoretically expected value.

Now only theoretical considerations speak for the assumption that the determinations of cardiac output were too high; as already mentioned, the W₁₇₀ determinations among our test subjects had been distinctly omitted, depending on their results either before or during the experiments, with simultaneous determination of the volume of cardiac output. The variation in both groups amounted to perhaps 10%. The reason was that, owing to arterial and venous puncture, the cardiac rate at rest was already around 13 min⁻¹ above these values prior to these sanguineous operations, and was also raised correspondingly with stress. These findings suppose that the boys tested by us

were in a situation of insignificant hyperkinetic circulation during the determination of cardiac output volume.

Worthy of note in this connection are the results of Emmrich et al., who discovered during research on adults of varying ages that cardiac rate and volume output at rest among the overwhelming majority of test subjects were clearly and persistently higher than before after the insertion of a venous catheter, and that in many instances a subsequent rise of both parameters due to an additional arterial puncture ensued. Bevegård et al., (1963) observed a rise in cardiac rate and in O_2 expenditure at rest as a consequence of inserting the catheters. Under stress, the influence of venous and arterial punctures on cardiac rate and O_2 intake could no longer be detected by the research staff, so that the W_{170} values were practically the same as before catheterization. We considered it was possible that the observed hyperkinetic variations in the circulatory situation among the children we tested under stress can be traced back to the research situation in the clinic, which was experienced as something exciting. /337

However, it in essence appears to us that, under comparable research conditions, not only do children with identical O_2 intake show lower volumes of cardiac output than adults, but according to our results, younger children transfer identical quantities of oxygen with smaller volumes of cardiac output even at rest and under stress than older children do. This means that the values of adults cannot be drawn on for a comparison with clinical experiments on the hemodynamic reaction of sick children at rest and during stress, but that as values for comparison those of healthy children of the same age would best suit the matter.

The explanation for the variable reaction of children compared with adults is probably that the organs which are not directly associated with the work exchange were perfused with relatively less blood among children than adults, so that a higher oxygen drain ensues here. This holds true as much for rest as for stress conditions. In contrast, it may be supposed that children of varying degrees of age and adults require identical quantities of blood in their working musculature under a given stress, so that no additional variations

arise with stress, but in essence the difference with respect to cardiac output volume, which was already present at rest, reappears on another level.

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